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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,939	02/05/2004	George N. Cox III	4152-1-PUS-7	7950

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EXAMINER	
DANG, IAN D	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/773,939	COX, GEORGE N.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-46* is/are pending in the application.

4a) Of the above claim(s) *24 and 26-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claim 25 in the communication filed on 09/14/2006 is acknowledged. In addition, Applicants further elect with traverse Group (A) a cysteine-reactive moiety.

The traversal is on the ground(s) that "unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility."

Applicants allege that all members of Claims 24, 25, and the Markush group of Claim 26 and related claims share the common utility of being useful for the general utilities as the wild-type IL-11 parent. In addition, Applicants assert that members of the Markush group share a substantial structural feature that is essential to that utility, which includes having a structure that is sufficiently similar to the wild-type sequence of SEQ ID NO:17 that the variants have IL-11 biological activity. Furthermore, Applicants allege the members all share the common structural feature of being cysteine variants, which provides the additional common utility of being readily modified to increase stability and half-life of the protein.

The argument is found not persuasive. The lack of unity cannot be applied to this instant application because it is a continuation of application 10/400,377 and is not a continuation from the 371 PCT/US98/14497. In addition, each member of the group does not share a substantial structural feature because the cysteine added variant may be inserted at different locations within the IL-11 sequence changing its structural feature. The addition of a cysteine variant at each different location will generate a new version of IL-11 with distinct structural features and biological activities. The amount of increased stability and half-life for IL-11 depend to the

location of the insertion of the cysteine variant and the type of modification for the cysteine-reactive moiety.

In addition, Applicants argue that the Examiner has not explained the restriction of Groups A-C and the groups are overlapping such that the restriction requirement does not make sense.

The argument is found not persuasive. The inserted cysteine residue can be modified with several cysteine-reactive moieties including more than one polyethylene glycol. Each cysteine reactive moiety is distinct from each other. The modification with each different moiety will generate distinct IL-11 structural characteristics and biological properties. Thus, each different cysteine-reactive moiety is distinct from the other.

Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05(c-I), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof: (B) A separate status in the art when they are classifiable together; (C) A different field of search." As set forth in the Restriction requirement, the separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Thus, the Restriction requirement is proper.

Applicant argues that no burden is placed on the examiner to consider all claims. As discussed above, the separate classification established for each Group demonstrates that each distinct Group requires a separate field of search, and a search of one Group would not reveal art on the other Groups, thus imposing a burden on the examiner. Furthermore, each group requires a non-coextensive sequence and non-patent literature search.

The requirement is still deemed proper and is therefore made FINAL. Claims 26-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

Claim 25 is pending and under examination.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 10/400,377 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The claimed invention drawn to a cysteine variant of interleukin-11, wherein a cysteine residue is inserted following the last amino acid of interleukin-11. The insertion of a cysteine residue following the last amino acid is not disclosed in the U.S. Application No. 10/400,377 or No. 09/462,941. Therefore, the instant application is given priority for the filing date of 02/05/2004.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Katre et al. (US Patent 5,206,344) in view of Harmegnies et al. (2003). The claimed invention is drawn to cysteine variant of interleukin-11 of SEQ ID NO:17, wherein a cysteine residue is inserted following the last amino acid of interleukin-11. The *in vitro* biological activity of the variant is measured by the proliferation of a cell line that proliferates in response to interleukin-11. Kartre et al. (US Patent 5,206,344) teach the modification of interleukin-2 wherein one of the non-cysteine amino acid residues of mature, native, human interleukin-2 is replaced by a cysteine residue. Katre et al. teach that modifying the interleukin with a cysteine at the end of the molecule allows for attachment of PEG or other polymers at a site that is not necessary for the biological activity of the molecule and increases serum half-life of the interleukin when administered *in vivo* (see the abstract and column 1, lines 40-60). Kartre et al. do not teach cystein mutagenesis of interleukin-11 and do not teach measuring the biological activity of the interleukin mutant *in vitro* by proliferation of a cell line, which is responsive to interleukin-11.

Harmegnies et al. teach that interleukin-11 is important as a potential therapeutic for a number of diseases (see abstract and page 23, column 1, first paragraph). Moreover, Harmegnies et al. teach that interleukin-11 can be mutated to increase its therapeutic efficacy (see the paragraph bridging pages 23-24 and page 31, last paragraph). Finally, Harmegnies et al. teach testing interleukin-11 muteins for enhanced activity *in vitro* by measuring the proliferation of 7TD1 (page 29, column 1, Figure 7).

It would have been prima facie obvious for one of ordinary skill in the art at the time of the invention was made to generate a cysteine variant of interleukin-11 wherein the cysteine residue is inserted following the last amino acid, as taught by Kartre et al., and to test the *in vitro* biological activity of the variant by measuring the proliferation of a cell line in response to interleukin-11, as taught by Harmegnies et al. One of ordinary skill in the art at the time the

invention was made would have been motivated to do so in order to make a potentially useful interleukin-11 mutein with enhanced serum half-life. Accordingly, the invention taken as a whole is *prima facie* obvious.

Conclusion

No claims are allowed.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang
Patent Examiner
Art Unit 1647
September 26, 2006

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